REMARKS

The Invention

In general, the present invention features substantially purified polypeptides consisting of a BAX ART domain and pharmaceutical compositions containing the same.

The Office action

Examination of claims 1-2, 6, 10, 14, 15, and 30-42 is reported in the present Office action. Claims 33, 34, 40, and 41 are drawn to a non-elected species and were not considered. Claims 1, 2, 6, 10, 14, 15, and 35 stand rejected under 35 U.S.C. § 102(e). Claims 1, 2, 6, 30-32, 35, and 36 stand rejected under 35 U.S.C. § 101. Claims 10, 14, 15, 37-39, and 42 are rejected under 35 U.S.C § 112, first paragraph. Claims 1, 2, 6, 10, 14, 15, and 35 stand rejected under 35 U.S.C. § 102(e), while claims 1, 2, 6, 10, and 35 are further rejected under 35 U.S.C. § 102(b). Each of these rejections is discussed in detail below.

Request for Withdrawal of Finality

As a preliminary matter, Applicants respectfully request that the finality of the present Office action be withdrawn. In support of Applicants' request, the Office is directed to M.P.E.P. § 706.07(a), which states:

> Under present practice, second or any subsequent actions on the merits shall be final, *except where the Examiner introduces a new ground of rejection* that is neither necessitated by applicant's amendment of the claims nor based on information submitted in an information disclosure statement filed

during the period set forth in 37 CFR 1.17 (p). (Emphasis added).

No significant amendment has been made to originally filed claim 10 that would necessitate the rejection of this claim (and claims dependent therefrom) for lack of enablement. Nor was any reference cited to the Office that would have provoked such a rejection. In short, the Office could have raised this rejection in the previous Office action, but failed to do so. Because the present rejection for lack of enablement forms a new ground of rejection that was neither necessitated by Applicants' amendments nor based on references submitted by Applicants in an information disclosure statement, Applicants respectfully request withdrawal of the finality of the present Office action.

Rejections under 35 U.S.C. § 101

Claims 1, 2, 6, 30-32, 35, and 36 are rejected under 35 U.S.C. § 101 as being directed to non-statutory subject matter. In particular, the Office states that the claims as written "do not particularly point out any non-naturally occurring differences between the claimed products and the naturally-occurring products." As requested by the Office, claim 1, from which the other rejected claims depend, has now been amended to recite polypeptides that are at least 60% pure by weight, thus clearly delineating these polypeptides from any that may naturally occur, and this rejection may now be withdrawn.

Rejections under 35 U.S.C. § 112, first paragraph

Claims 10, 14, 15, 37-39, and 42 are rejected under 35 U.S.C. § 112, first paragraph, for lack of enablement. In applying this rejection, the Office contends that the specification, while being enabling for a polypeptide containing SEQ ID NO: 1 or 3, is not enabling for a pharmaceutical composition containing such polypeptides.

As an initial matter, Applicants note that, contrary to the Office's assertion, claim 10 is not limited to compositions containing SEQ ID NOs: 1 or 3. Rather, the claim 10 directed to pharmaceutical compositions containing polypeptides consisting of a BAX ART domain. Claim 10 (as well as claim 1, which the Office also improperly construed as being limited to SEQ ID NOs: 1 or 3) is a linking claim (linking polypeptides consisting of SEQ ID NOs: 3, 4, or 5). M.P.E.P. § 809 states that "[t]he linking claims must be examined with the invention, and should any linking claim be allowed, the restriction requirement must be withdrawn." Accordingly, Applicants respectfully request that claims 1 and 10 be examined to their full scope.

Turning now to the enablement rejection, the Office asserts that the specification, in teaching that administration of a BAX ART polypeptide prevents apoptosis, fails to teach "how the polypeptide of the invention would be administered, the bioavailability of the peptide at the site of interest, how the peptide is to translocate into the cell, and the immune responses generated from the administration of the peptide." Citing Jain (*Sci. Am.* (1994) 271:58-65) and Dermer (*Biotechnology* (1994) 12:320), the Office supports this rejection by highlighting the unpredictability of peptide administration *in vivo* and

concludes that one skilled in the art would not be able to practice the claimed invention in the absence of undue experimentation. Applicants respectfully traverse this rejection for the reasons outlined below.

Applicants first note that the Office, in applying this rejection, has failed to provide support for doubting the inaccuracy of the present disclosure. Because Applicants have provided teachings (discussed in greater detail below) enabling the claimed invention throughout the specification, the burden is on the Examiner to provide evidence or reasoning to the contrary. This burden is set forth in the Guidelines for the Examination of Patent Applications under 35 U.S.C. § 112, first paragraph, "Enablement" requirement, which states:

> A specification disclosure which contains a teaching of the manner and process of making and using an invention in terms which correspond in scope to those used in describing and defining the subject manner sought to be patented must be taken as being in compliance with the enablement requirement of 35 U.S.C. § 112, first paragraph, unless there is a reason to doubt the objective truth of the statements contained therein which must be relied on for enabling support. Assuming that sufficient reason for such doubt exists, a rejection for failure to teach how to make and/or use will be proper on that basis. *In re Marzocchi*, 439 F.2d 220, 224, 169 USPQ 367, 370 (CCPA 1971). As stated by the court, "it is incumbent upon the Patent Office, whenever a rejection on this basis is made, to explain *why* it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement. Otherwise, there would be no need for the applicant to go to the trouble and expense of supporting his presumptively accurate disclosure." 439 F.2d at 224, 169 USPQ at 370.

Although the Office has relied on two independent references to support the present lack of enablement rejection, Applicants assert that these references do not in fact provide sufficient evidence or reasoning to satisfy the Examiner's burden. First, Applicants note that both Jain and Dermer were published in 1994, seven years prior to Applicants' filing date. Applicants assert that such disclosures do not appropriately represent the state of the prior art at the time of filing and thus, cannot be considered as sufficient evidence to support a lack of enablement rejection. Secondly, Applicants submit that Jain and Dermer, while teaching the inefficacy of drug delivery, are both directed to the treatment of cancer. In this regard, both references emphasize that the difficulties faced by the administration of anti-cancer treatments are primarily caused by properties unique to tumors. Jain states, for example, that "a much overlooked property of tumors–namely resistance to penetration of drugs--can play a significant role in undermining therapy... The likelihood that tumors could impede drug penetration was suggested partly by their structure." Clearly, these problems are not relevant to the present invention, in which the administration of BAX ART polypeptides would result in a decrease in apoptosis (rather than in an increase). BAX ART polypeptides are pro-survival polypeptides and, consequently, would not be appropriate for the treatment of cancer. Because Jain and Dermer focus exclusively on the difficulties of administering anti-cancer drugs, and because BAX ART polypeptides are not such drugs, these references do not provide sufficient evidence to support the lack of enablement rejection.

Notwithstanding the Office's failure to meet its burden, Applicants submit that a use of the BAX ART polypeptide-containing compositions is enabled by the specification. Contrary to the Office's assumption, one skilled in the art seeking to make and use the claimed invention may not necessarily administer the peptide for the sole purpose of decreasing apoptosis. On this point, Applicants direct the Office to page 15, lines 4-14, which states:

> Antibodies (*e.g.*, polyclonal, monoclonal, single chain, humanized, chimeric) that are specific toward either a BAX ART domain or a BAX TM domain may be generated using a BAX ART domain-containing polypeptide fragment or a BAX TM-domain containing polypeptide fragment, respectively, as an antigen. Conversely, the entire BAX protein may be used as antigen, and the antibodies subsequently screened for an ability to specifically bind the ART domain or the TM domain. Standard methods for producing antibodies are well known in the art (see, *e.g.*, Ladner, U.S. Patent No. 4,946,778; Current Protocols in Immunology, ed. J.E. Coligan, John Wiley & Sons, New York, NY, 1991; Ward et al., Nature 341:544-546, 1989; Green et al., Nature Genetics 7:13-21, 1994; Cabilly et al., U.S. Patent No. 4,816,567; Boss et al., U.S. Patent No. 4,816,397).

One skilled in the art reading the specification would understand that, in addition to decreasing apoptosis, a polypeptide consisting of a BAX ART may also serve as an antigen and may therefore be administered *in vivo* to produce antibodies specific to the BAX ART domain. One of skilled in the art would further understand that the production of such antibodies would merely require using techniques taught in the specification and/or known in the art. M.P.E.P. § 2164.01(c) states that "if any use is enabled when multiple uses are disclosed, the application is enabling for the claimed invention." Applicants submit that such requirement has been met, and withdrawal of the § 112, first

paragraph rejection is respectfully requested.

Rejections under 35 U.S.C. § 102

Claims 1, 2, 6, 10, 14, 15, and 35 stand rejected under 35 U.S.C. § 102(e) as being anticipated by Korsmeyer *et al.,* (U.S.P.N. 5,691,179, hereinafter "Korsmeyer"). Claims 1, 2, 6, 10, and 35 are rejected under 35 U.S.C. § 102(b) as being anticipated by Apte *et al.* (*Genomics* (1995) 26:592-594, hereinafter "Apte") and by Oltvai *et al.* (*Cell* (1993) 74:609-619; hereinafter "Oltvai").

Applicants again note that the Office has improperly limited the scope of claims 1 and 10 to those polypeptides containing SEQ ID NO: 1 or SEQ ID NO: 3. As discussed above, contrary to the Office's assertion that "the claims are drawn to a polypeptide consisting essentially or has a BAX ART domain wherein the BAX ART domain is represented by the motif of SEQ ID NO: 1 and/or has the sequence of SEQ ID NO: 3," Applicants note that neither claim is so limited, and examination of these claims to their full scope is respectfully requested.

Turning now to the rejection, based on recitation of the term "consisting essentially of" in the rejected claims, the Office asserts that the claimed polypeptides would include the polypeptides disclosed by Korsmeyer, Apte, and Oltvai. As amended, claim 1, from which claims 2, 6, and 35 depend, and claim 10, from which claims 14 and 15 depend, are now directed to polypeptides "consisting" of a BAX ART domain. Because none of the cited references teach such polypeptides, the rejection of claims 1, 2,

6, 10, 14, 15, and 35 as being anticipated by Korsmeyer, Apte, and/or Oltvai may now be withdrawn.

CONCLUSION

Applicants submit that the claims are now in condition for allowance and such action is respectfully requested.

Applicants further note that the Form PTO-1449 that was submitted with an Information Disclosure Statement filed on June 6, 2001 has not been initialed and returned, and hereby request that it be initialed and returned with the next Office action.

If there are any charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

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